PHOTOREACTION OF α, β – ENONES IN METHANOL IN THE PRESENCE OF TITANIUM (IV) CHLORIDE

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ABSTRACT

When cyclic α, β-unsaturated carbonyl compounds were irradiated by ultraviolet from a high pressure mercury vapour lamp at 25 °C, in alcohols in the presence of titanium chloride, a coupling reaction between the carbonyl carbon atom and the α-carbon atom of the alcohol took place, producing dihydrofurans, monomethylether, acetals or aldehides, but in the case of α-methyl substituted enone it resulted in diol monomethylether due the two times occuring methanol substitution.

INTISARI

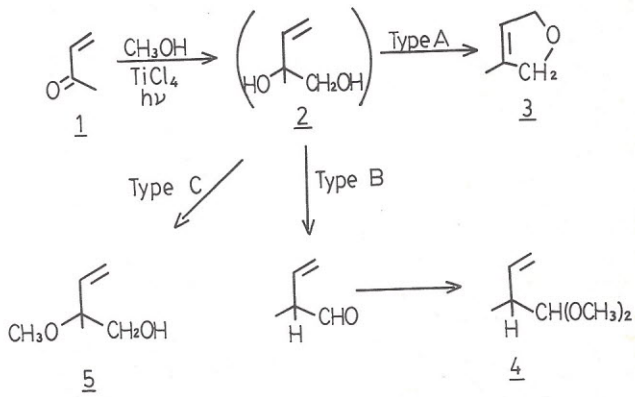
Bila senyawa karbonil siklik α, β-tak jenuh diradiasi dengan ultra-violet dari lampu merkuri bertekanan tinggi pada 25 °C dalam alkohol dengan titanium klorida, reaksi penggabungan antara atom karbon karbonil dan atom α-karbon dari alkohol membentuk senyawa dihidrofuran, monometileter, asetal atau aldehida, tetapi jika senyawa enone yang tersubstitusi pada α-metil akan menghasilkan diol dari monometileter akibat substitusi metanol yang terjadi secara dua kali.

INTRODUCTION

Photoreaction in the presence of $TiCl_4$

Sato reported α, β-unsaturated ketones, when irradiated in alcohols in the presence of titanium(IV) chloride, underwent novel types of reactions with the formation of a C–C bond between the carbonyl carbon atom and the α-carbon atom of the alcohols(1). Hart(2) classified the reactions of α, β-unsaturated ketones into six types: (i) β-or γ-hydrogen abstraction, (ii) dimerization to cyclobutane, (iii) inter- or intra-molecular oxetan formation, (iv) isomerization to 'lumi-product', (v) cis-trans isomerization, and (vi) type I cleavage. Coupling with solvent molecules has received less attention, although a few examples have been described (3). As a typical example, the $TiCl_4$-catalyzed reactions of α, β-enones (*1*) with methanol are shown in Scheme I. Depending upon the types of the substrated, the $TiCl_4$-catalyzed photo-reaction gave three types of products: dihydrofurans (*3*) (type A), acetals (*4*) (type B), and 1,2-diolmonomethylethers (*5*) (type C). All the products are considered to be derived from a common intermediate, 1, 2-diol (*2*), which is formed through the 1, 2-addition of methanol to the carbonyl group.

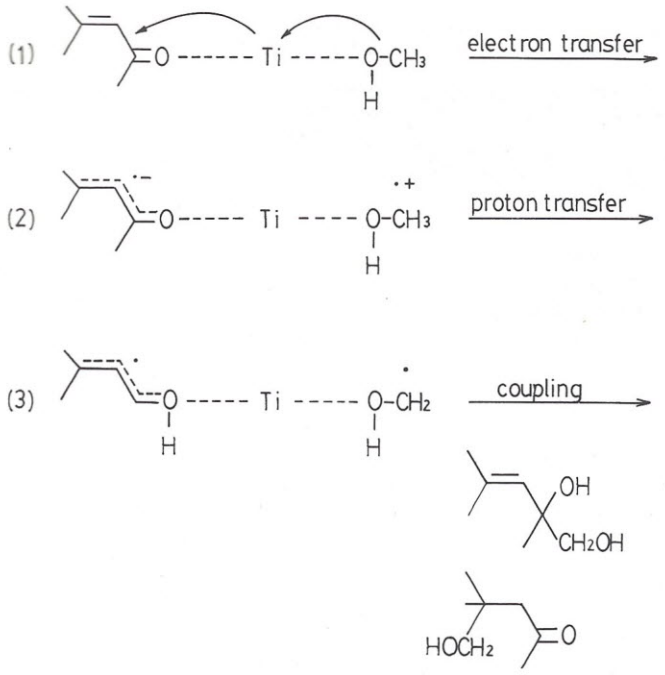
All the reactions (types A-C) can be shown schematically to involve a step of the formal coupling of the hydroxymethyl radical with the carbonyl carbon (1,2 type) or the olefinic β-carbon (1,4 type) of the enones. However, the present reaction is characteristic in several features(4). (*1*) 1, 2-Addition of methanol to enones as observed in the $TiCl_4$-catalyzed reaction is quite unusual. It is



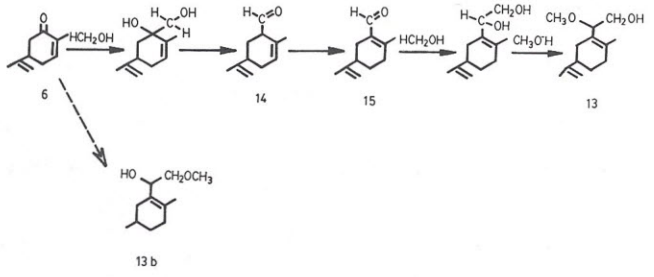
Scheme I

known that most of the alcohol or ether additions to enones through the use of UV irradiation, if they ever proceed, give 1,4 type products. (*2*) Although hydrogen abstraction by a ketone from an alcohol is well known, cross coupling to form a mixed pinacol is rare, ketyl-radical dimerization is usually preferable. (*3*) The reactivities of alcohols with ethyl 2-butenoate in the benzophenone-sensitized coupling reaction have been reported to increase in the order methanol < ethanol < 2-propanol, while the order of the reactivities of the alcohols in the present reaction was found to be completely reversed. These observations induced Sato to propose a mechanism other than that involving radical species, and we have suggested (4) a mechanism (Scheme II) comprising of (*1*) a metal-assisted and photoassisted electron transfer from the alcohol to the carbonyl compound, (*2*) the succeeding proton transfer from the alcohol radical cation to the enone radical anion, imparting a radical character to the α-carbon atom of the alcohol and the carbonyl carbon atom of the enone, and (*3*) the coupling of the radicals to form a new C–C bond. All these process are considered to be proceeding consecutively in a close vicinity on the metal ion, thus providing a circumstance favorable for the cross coupling. Evidence for this type of electron transfer among ligands on a metal ion was recently obtained, and the details of the mechanism, which is termed as a "long-range electron-transfer mechanism" have been discussed by others.(5).

In the present study, we found that the reaction is applicable to other types of compound. For 2-cyclohexene-1-one with β substituent, the reaction in methanol afforded aldehyde (*7*) and acetal (*8*) as the main product. Now we found that the reaction of 2-cyclohexene-1-one (run ③) in methanol afforded (*11*) as the main product and small amount of acetal (*12*). Similarly, carvone



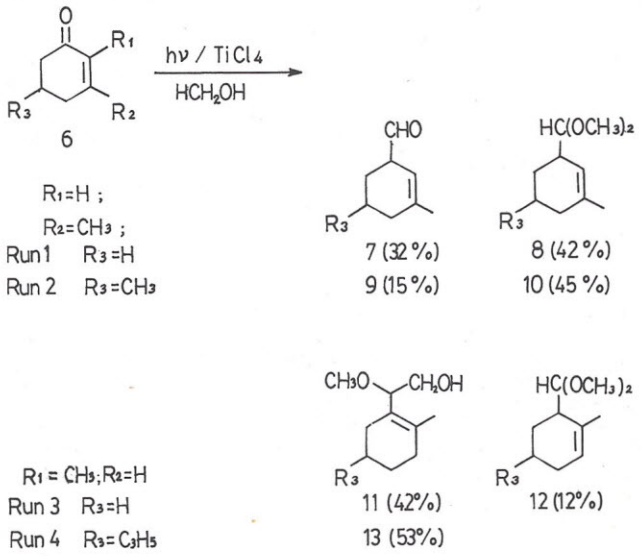
Scheme II

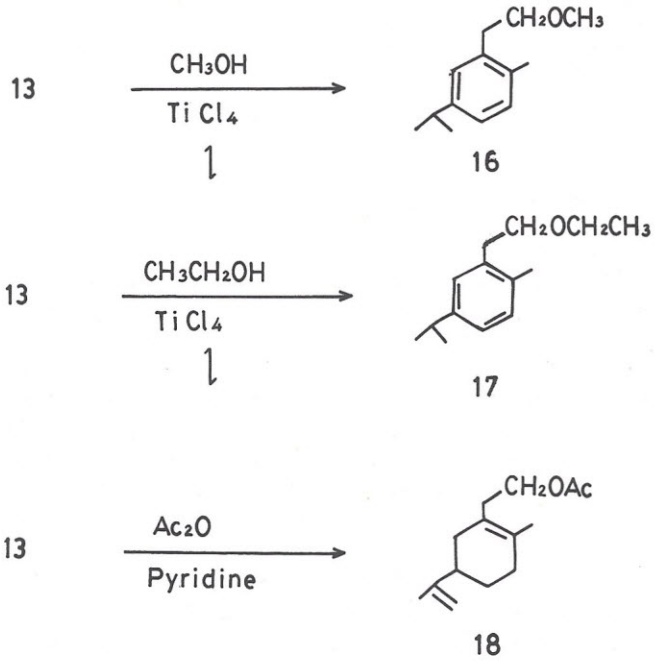


Scheme III

(run ④) gave (*13*) as the main product. This is an *unusual* reaction in which two molecules of methanol took part in the reaction in the present of $TiCl_4$ (Scheme III). The reaction could be schemed as proceeding in the same way as usual to produce aldehyde (*14*) followed by double bond migration to the stabile position to give (*15*). The unsaturated aldehyde again underwent the same type of reaction to give (*13*) as the main product. When (*13*) was refluxed in methanol with $TiCl_4$ as catalyst, an aromatic product (*16*) was obtained.

The NMR spectra of (*16*) at δ 2.5-3.8 showed A_2B_2 pattern, indicating the participation of two molecules of methanol in the C-C bond formation, ^{13}C spectrum of (*13*) indicated that each carbon atom showed a pair of signal which indicated that (*13*) consisted of two diastereomers. When refluxed in ethanol with catalyst $TiCl_4$, (*13*) gave (*17*). The formation of (*16*) from (*13*) in methanol/$TiCl_4$ leaves the possibility that the primary product might be (*13b*), rather than (*13*). This was ruled out because (*17*) was obtained when (*13*) was refluxed in ethanol. Evidently the methoxyl group in (*16*) was introduced at the second stage reaction. As another evidence to confirm the position of the methoxyl and hydroxyl, (*13*) was acetylated to produce (*18*). The chemical shifts of methine proton around δ 4.2 did not shift up on acetylation, but the chemical shifts of the methylene proton around δ 3.5 shifted 0,5 ppm down field. The results confirmed the structure of (*13*). From the results, we can confirm that the photoreaction of α, β-enone with methyl substituted at a position in methanol, proceeds with the participation of two molecules of methanol in the C-C bond formation.





EXPERIMENTAL METHODS

Chemicals:

Pro analysis grade of chemicals were used for all experiment.

Equipment:

Mass spectra were obtained with Hitachi RMS-4 spectrometer IR spectra with a Perkin Elmer 1600 series FT-IR spectrometer, and NMR spectra with a JEOL JNM-PMX-60 SI (60

MHz), Hitachi R-90H (90 MHz) Fourier Transform NMR-spectrometer (Me_4Si as internal standard) (7). GLC analysis were carried out with a Shimadzu GC-8A gas chromatograph fitted with a 2.5 m x 6 mm stainless column packed with Silicone SE 30, and Shimadzu GCMS-QP-1000, Shimadzu GC-9A.

Experimental

All irradiation were carried out in solutions in Pyrex tubes with a high pressure mercury vapour lamp (Riko UVL-100HA (100 W) or Ushio UM-452 (450 W)) at running-water temperature (± 25 °C) (7). After the irradiation, the solution was poured into water and shaken with dichloromethane. The extract was dried with anhydrous Na_2SO_4 and the solvent was removed in *vacuo.* The residual oil was treated as indicated in figure 1 (carousel assembly) (8).

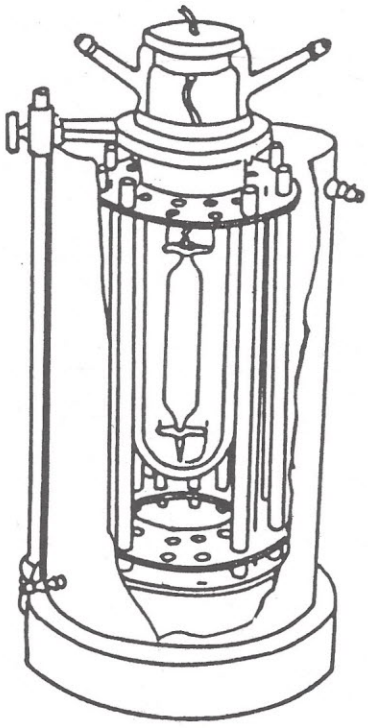


Figure 1 Carousel Assembly(8)

Photolysis of 3-methyl-2-cyclohexeone (Run ①) in Methanol-$TiCl_4$. A solution of 3-methyl-2-cyclohexenone (1 g) and titanium tetrachloride concentrate (1 ml) in methanol (100 ml) was irradiated for 7 h. The yield was an oil (1.1 g) shown to be mixture of compounds (7) (32%), (8) (42%) from NMR and GLC analysis. Both were separated by silica gel column chromatography.

(7) : NMR δ 1.70 (s, 3H), 1.50-2.50 (br, 7H), 5.50 (s, 1H), 9.40 (d, J=2Hz, 1H)

(8) : NMR δ 1.70 (s, 3H), 1.50-2.50 (br, 7H), 3.25 (s, 6H), 4.0 (d, J=8Hz, 1H), 5. 3 (s, 1H)

Photolysis of 3,5-dimethyl-2-cyclohexenone (Run ②) in Methanol-$TiCl_4$. A solution of 3, 5-dimethyl-2-cyclohexenone (1, 35 g) and titanium tetrachloride (1.2 ml) in methanol (100 ml) was irradiated for 7 h. A crude oil (1.27 g) was obtained which was chromatographed on a silica gel column to give compounds (9) (15%) and (10) (46%).

(9) : NMR δ 1.10 (s, 3H), 1 50-2.30 (br), 1.60 (s, 3H), 5.30 (s, 1H), 9.40 (d, J=2Hz, 1H).

(10): NMR δ 1.05 (s, 3H), 1.60-2. 0 (br), 1.60 (s, 3H), 3.25 (s, 6H), 3.9 (s, 1H), 5.3 (s, 1H)

Photolysis of 2-methyl-2-cyclohexenone (Run ③). A solution of 2-methyl-2-cyclohexenone (0.6 g) and titanium tetrachloride (0. 6 ml) in methanol (60 ml) was irradiated for 7h. A crude oil (0.61 g) was obtained which was chromatographed on a silica gel column to give compounds (11) (42%) and (12) (12%).

(11) : NMR δ 1.50-2.20 (br, 8H), 1.70 (s, 3H), 3.10-3.50 (m, 2H), 3.20 (s, 3H), 4.20 (q, J=4Hz, 1H), 5.40 (s, 1H).

(12) : NMR δ 1.50-2.20 (br, 7H), 1.70 (s, 3H), 3.20 (2s, 6H), 4.20 (q, J=6Hz, 1H), 5.40 (s, 1H).

Photolysis of Carvone in Methanol-$TiCl_4$ (Run ④). A solution of carvone (1.1 g) and $TiCl_4$ (1.2 ml) in methanol (120 ml) was irradiated for 7 h. The yield was an oil (1.07 g) which was compound (13) (53%) after purification by silica gel column-chromatography.

(13) : IR, 3425 cm^{-1}, NMR δ 1.70 (s, 6H), 1.60-2.40 (br, 7H), 3.25 (d, J=4Hz, 2H), 3.20 (s, 3H), 4.0-4.30 (t, 1H), 4.70 (s, 2H).
^{13}C-NMR δ 149, 132, 126, 100, 81, 64, 56, 41, 33, 29, 27, 20, 18.

Treatment of (13) in $TiCl_4$. A mixture of compound (13) (0.1 g), $TiCl_4$ (0.1 ml) and methanol (10 ml) was refluxed for 3 h. Subsequent extraction with dichlormethane gave compound (16) (0.089 g).

(16) : IR, 1502, 1458, 1381, 1362, 1114, 818 cm^{-1}. NMR δ 1.20 (s, 6H), 2.20 (s, 3H), 2.70-3.60 (m, 4H), 3.10-3.2 (m, 1H), 3.20 (s, 3H), 6.90 (s, 3H),

when compound (13) was refluxed in ethanol, it produced compound (17).

(17) : NMR δ 1.10 (d, J=6Hz, 6H), 1.20 (t, 3H), 1.10-2.50 (m), 2.80 (t, 2H), 3.20-3.80 (m, 4H), 7.0 (s, 3H).

Acetylation of (13). A mixture of compound (13) (0.08 g), acetic acid anhydride (0.3 ml), in pyridine (8 ml) was stirred for 3h. Subsequent extraction with dichlormethane produced compound (17) (50 mg).

(18) : IR, 1743, 1233 cm^{-1}. NMR δ 1.70 (s, 6H), 1.90-2.10 (br, 7H), 2.0 (s, 3H), 3.20 (2s, 3H), 3.90-4.20 (br, 1H), 4.10 (s, 2H).

(15) : NMR δ 1.10-2.50 (br), 3.20 (s, 3H), 3.60 (s, 1H).

(16) : NMR δ 1.50-2.50 (br. 7H), 3.20 (2s, 6H), 4.0 (d, J=8Hz, 1H), 5,60 (s, 2H).

III. RESULTS AND DISCUSSION

When α, β cyclohexenone was irradiated in methanol in the presence of titanium (IV) chloride, aldehyde and acetal were isolated as the main products. This is a normal reaction similar to those reported previously, in which one molecule of alcohol takes a part in the reaction. In the present study, we described that cyclohexenone with methyl substituent at α position gave another type of product, involving two molecules of methanol to produce compound (11) as the main product from 2-methyl cyclohexenone and compound (13) from carvone. When compound (13) was refluxed in methanol with $TiCl_4$ as catalyst, an aromatic product compound (16) was obtained. The NMR spectra of compound (16) at δ 2.5-3.8 showed A_2B_2 pattern, indicating the participation of two molecules of methanol in the C-C bond formation. ^{13}C

spectrum of compound indicated that each carbon atom showed a pair of signal which indicated that compound consisted of two diastereomers. When refluxed in ethanol with catalyst $TiCl_4$, compound gave compound (*17*). The formation of compound (*16*) from compound in methanol/$TiCl_4$ leaves the possibility that the primary product might be compound (*13b*), rather than compound (*13*). This was ruled out because compound (*17*) was obtained when compound (*13*) was refluxed in ethanol. Evidently the methoxyl group in compound (*16*) was introduced at the second stage reaction. As another evidence to confirm the position of the methoxyl and hydroxyl, compound (*13*) was acetylated to produce compound (*18*). The chemical shifts of methine proton around δ 4.2 did not shift upon acetylation, but the chemical shifts of the methylene proton around δ 3.5 shifte 0.5 ppm down field. The result confirmed the structure of compound (*13*). From this reaction we can understand that photoreaction of α, β-enone with methyl substituted at α position proceeds with participation of two molecules of alcohols in methanol.

We think that the photoreaction of α, β-enone with methyl substituted at α position proceeds in methanol through the path shown in scheme III.

IV. CONCLUSION

Photoreaction of cyclic α, β-enones with methanol in the presence of titanium (IV) chloride was reported as a novel type reaction, it proceeded with the formation of C-C bond between the carbonyl carbon atom and the α-carbon atom of methanol. As a typycal example, the $TiCl_4$ catalyzed reaction of α, β-enones with methanol gave three types of products : dihydrofurans, unsaturated β, γ-aldehyde-acetals and 1,2-diolmonomethylesters. In this reactions, the $TiCl_4$ catalyst induced the reaction of the substrated with one molecule of methanol. Furthermore for α, β-unsaturated ketones with β-substitution, the reaction went normally, producing aldehyde and acetal, but with α-substitution, for example carvone, the irradiation in the present of $TiCl_4$, induced two molecules of methanol to participate in the reaction. The reaction to cyclohexenone with no substituent in methanol gave another product of 3-methoxycyclohexane as the main product and a small amount of acetal form, in order to confirm reaction mechanism in scheme III.

The results of the study conclude that when α, β-enones were irradiated in methanol in the present of $TiCl_4$ the products obtained depend on the position of the substituent. Substrates having methyl in β-position gave aldehyde and acetal as reaction products in methanol. However, when methyl group is in α-position, two molecules of methanol are involved in the C-C bond formation.

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